

Bölüm 11

SERVİKS KANSERİNDE EPİDEMİYOLOJİ RİSK FAKTÖRLERİ VE KLİNİK

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GİRİŞ

Serviks kanseri dünya çapında en sık ölüme yol açan kanserler arasında üçüncü sırada yer almaktadır (Siegel& ark. 2018). Uterin korpus kanserleri ve ovaryen kanserlere oranla, gelişmiş ülkelerde, daha az mortalite insidansına sahiptir (Torre & ark. 2012). Ancak henüz serviks kanseri tarama programı bulunmayan ülkelerde halen kanser nedeni ölümlerde 9.8/ 100000 oranıyla ve ensik görülen kanserlerde 17.8/ 100000 oranıyla ikinci sırayı almaktadır.

Servikal kanserlerin %99.7'sinden ve servikal intraepitelyal neoplazilerin gelişiminden human papillomavirus (HPV) sorumlu tutulmaktadır (Walboomer& ark. 1999). En sık görülen serviks kanseri histopatolojisi %69 ile yassı hücreli karsinom ve %25 ile adenokarsinomdur (Ries& ark. 2007).

EPİDEMİYOLOJİ VE RİSK FAKTÖRLERİ

Tümdünyadaki insidansı ve mortalitesi, prekanseröz lezyonların ve HPV enfeksiyonunun tarama programlarıyla tanı alması ve tedavi edilmesi ayrıca HPV aşısının yaygınlaşması sebebiyle gelişmiş ülkelerde başta olmak üzere azalmaktadır. Gelişmiş ülkelerde son 50 yılın verileriyle karşılaştırıldığında servikal kanserin mortalitesinde ve insidansında %75'e yakın bir azalma gözlenmektedir (Quinn& ark. 1999, Willoughby & ark. 2006). Servikal kanser vakalarının %84 kadarı az gelişmiş bölgelerden çıkmaktadır (Torre & ark. 2012).

YAŞ

Amerika'daki kadınlarda yaşam boyu serviks kanseri gelişme riski 2000-2004 yılları arasında %0.76 olarak hesaplanmıştır ve serviks kanseri ortalama tanı yaşı 48'dir (4). 20 yaş altındaki kızlarda 0.1/100000, 20-24 yaş arasında 1.5/100000, 30-35 yaş arasında 11.0-15.8/100000 ve 35 yaş > vakaların %5.7'si serviks kanserini almaktadır.

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Serviks kanser taramasında servikalsitoloji testi ve HPV testi kombine kullanılmaktadır. Malinite semptomları olan ya da gözle görülebilen tümörü olan kadınlarda kullanılmamaktadır.

Servikal biyopsi ve kolposkopi

Servikal biyopsi malignite düşünülen hastalarda başlangıçta yapılanışlemdir. Hastanın pelvik muayenesinin ardından şüpheli bölgeden biyopsi alınmalıdır.

Gözle görülebilen lezyon varlığında, kanser tanısı şüphesini doğrulamak adına lezyonda biyopsi alınmalıdır. Biyopsi, en şüpheli görünen alandan alınmalı, nekrotik alandan mümkün oldukça alınmamalıdır. Serviks normalden gergin ya da büyükse punch biyopsi alınmalı ve endoservikal küretaj yapılmalıdır. Bu durumlarda servikal sitolojinin değeri yoktur. Biyopsi sonrası meydana gelen kanamalarda Monsel solüsyonu kullanılabilir.

Gözle görülen lezyonu olmayan kadınlarda (semptomatik anormal servikal sitoloji) kolposkopi eşliğinde biyopsi alınmalıdır.

Semptomatik ancak gözle görülen lezyonu olmayan kadınlarda anormal sitoloji varlığında kolposkopi alında direkt servikal biyopsi alınmalıdır. Kolposkopide skuamokolumnar bileşke ve lezyon gözlenmeli bu bölgelerden biyopsi alınmalıdır. Kolposkopi imkanıyoksa direkt biyopsi alınabilir ya da VIM (visual inspection methods) ile alınabilir.

Maliniteden şüphelenildi ancak direkt servikal biyopside bulunamadı ve servikalkonizasyon gerekli ise (HGSIL high grade cervical intraepithelial neoplasi-aendoservikal küretaj pozitif displaziler), konizasyon mikroinvaziv kanserleri tanımda ve konservatif tedavisinde ya da radikal cerrahi öncesinde yol gösterici olarak kullanılabilen bir metottur.

KAYNAKLAR

- Anttila T, Saikku P, Koskela P, et al. Serotypes of Chlamydia trachomatis and risk for development of cervical squamous cell carcinoma. JAMA 2001; 285:47.
- Arends MJ, Buckley CH, Wells M. Aetiology, pathogenesis, and pathology of cervical neoplasia. J Clin Pathol 1998; 51:96.
- Castellsagué X, Bosch FX, Muñoz N, et al. Male circumcision, penile human papillomavirus infection, and cervical cancer in female partners. N Engl J Med 2002; 346:1105.
- Castle PE, Wacholder S, Lorincz AT, et al. A prospective study of high-grade cervical neoplasia risk among human papillomavirus-infected women. J Natl Cancer Inst 2002; 94:1406.
- Craveiro R, Bravo I, Catarino R, et al. The role of p73 G4C14-to-A4T14 polymorphism in the susceptibility to cervical cancer. DNA Cell Biol 2012; 31:224.
- DiSaia PJ, Creasman WT. Invasive cervical cancer. In: Clinical Gynecologic Oncology, 7th ed., Mosby Elsevier, Philadelphia 2007. p.55.

- Franco EL, Schlecht NF, Saslow D. The epidemiology of cervical cancer. *Cancer J* 2003; 9:348.
- Gierisch JM, Coeytaux RR, Urrutia RP, et al. Oral contraceptive use and risk of breast, cervical, colorectal, and endometrial cancers: a systematic review. *Cancer Epidemiol Biomarkers Prev* 2013; 22:1931.
- Green J, Berrington de Gonzalez A, Sweetland S, et al. Risk factors for adenocarcinoma and squamous cell carcinoma of the cervix in women aged 20-44 years: the UK National Case-Control Study of Cervical Cancer. *Br J Cancer* 2003; 89:2078.
- Grimm C, Watrowski R, Baumühlner K, et al. Genetic variations of interleukin-1 and -6 genes and risk of cervical intraepithelial neoplasia. *Gynecol Oncol* 2011; 121:537.
- Hawes SE, Kiviat NB. Are genital infections and inflammation cofactors in the pathogenesis of invasive cervical cancer? *J Natl Cancer Inst* 2002; 94:1592.
- Hemminki K, Chen B. Familial risks for cervical tumors in full and half siblings: etiologic apportioning. *Cancer Epidemiol Biomarkers Prev* 2006; 15:1413.
- Hughes RR, Brewington KC, Hanjani P, et al. Extended field irradiation for cervical cancer based on surgical staging. *Gynecol Oncol* 1980; 9:153.
- International Collaboration of Epidemiological Studies of Cervical Cancer. Comparison of risk factors for invasive squamous cell carcinoma and adenocarcinoma of the cervix: collaborative reanalysis of individual data on 8,097 women with squamous cell carcinoma and 1,374 women with adenocarcinoma from 12 epidemiological studies. *Int J Cancer* 2007; 120:885.
- International Collaboration of Epidemiological Studies of Cervical Cancer, Appleby P, Beral V, et al. Carcinoma of the cervix and tobacco smoking: collaborative reanalysis of individual data on 13,541 women with carcinoma of the cervix and 23,017 women without carcinoma of the cervix from 23 epidemiological studies. *Int J Cancer* 2006; 118:1481.
- International Collaboration of Epidemiological Studies of Cervical Cancer. Cervical carcinoma and reproductive factors: collaborative reanalysis of individual data on 16,563 women with cervical carcinoma and 33,542 women without cervical carcinoma from 25 epidemiological studies. *Int J Cancer* 2006; 119:1108.
- International Collaboration of Epidemiological Studies of Cervical Cancer, Appleby P, Beral V, et al. Cervical cancer and hormonal contraceptives: collaborative reanalysis of individual data for 16,573 women with cervical cancer and 35,509 women without cervical cancer from 24 epidemiological studies. *Lancet* 2007; 370:1609.
- Jones C. Cervical cancer: is herpes simplex virus type II a cofactor? *Clin Microbiol Rev* 1995; 8:549.
- Kayes O, Ahmed HU, Arya M, Minhas S. Molecular and genetic pathways in penile cancer. *Lancet Oncol* 2007; 8:420.
- Kjaer SK, de Villiers EM, Cağlayan H, et al. Human papillomavirus, herpes simplex virus and other potential risk factors for cervical cancer in a high-risk area (Greenland) and a low-risk area (Denmark)--a second look. *Br J Cancer* 1993; 67:830.
- Lagasse LD, Creasman WT, Shingleton HM, et al. Results and complications of operative staging in cervical cancer: experience of the Gynecologic Oncology Group. *Gynecol Oncol* 1980; 9:90.
- Lee YN, Wang KL, Lin MH, et al. Radical hysterectomy with pelvic lymph node dissection for treatment of cervical cancer: a clinical review of 954 cases. *Gynecol Oncol* 1989; 32:135.

- Lehtinen M, Koskela P, Jellum E, et al. Herpes simplex virus and risk of cervical cancer: a longitudinal, nested case-control study in the nordic countries. *Am J Epidemiol* 2002; 156:687.
- Li N, Franceschi S, Howell-Jones R, et al. Human papillomavirus type distribution in 30,848 invasive cervical cancers worldwide: Variation by geographical region, histological type and year of publication. *Int J Cancer* 2011; 128:927.
- Liu L, Yang X, Chen X, et al. Association between TNF- α polymorphisms and cervical cancer risk: a meta-analysis. *Mol Biol Rep* 2012; 39:2683.
- Manhart LE, Holmes KK, Koutsky LA, et al. Human papillomavirus infection among sexually active young women in the United States: Implications for developing a vaccination strategy. *Sex Transm Dis* 2006; 33:502.
- Metcalf KS, Johnson N, Calvert S, Peel KR. Site specific lymph node metastasis in carcinoma of the cervix: Is there a sentinel node? *Int J Gynecol Cancer* 2000; 10:411.
- Muñoz N, Franceschi S, Bosetti C, et al. Role of parity and human papillomavirus in cervical cancer: the IARC multicentric case-control study. *Lancet* 2002; 359:1093.
- Parkin DM, Bray F. Chapter 2: The burden of HPV-related cancers. *Vaccine* 2006; 24 Suppl 3:S3/11.
- Pilleron JP, Durand JC, Hamelin JP. Prognostic value of node metastasis in cancer of the uterine cervix. *Am J Obstet Gynecol* 1974; 119:458.
- Quinn M, Babb P, Jones J, Allen E. Effect of screening on incidence of and mortality from cancer of cervix in England: evaluation based on routinely collected statistics. *BMJ* 1999; 318:904.
- Ries LAG, Melbert D, Krapcho M, et al. SEER Cancer Statistics Review, 1975-2004. National Cancer Institute; Bethesda, MD 2007.
- Saraiya M, Ahmed F, Krishnan S, et al. Cervical cancer incidence in a prevaccine era in the United States, 1998-2002. *Obstet Gynecol* 2007; 109:360.
- Schiffman M, Castle PE, Jeronimo J, et al. Human papillomavirus and cervical cancer. *Lancet* 2007; 370:890.
- Sevin BU, Nadji M, Averette HE, et al. Microinvasive carcinoma of the cervix. *Cancer* 1992; 70:2121.
- Siegel RL, Miller KD, Jemal A. Cancer statistics, 2018. *CA Cancer J Clin* 2018; 68:7.
- Singh GK, Miller BA, Hankey BF, Edwards BK. Area Socioeconomic Variations in U.S. Cancer Incidence, 1975-1999. National Cancer Institute; Bethesda, MD 2003.
- Smith JS, Herrero R, Bosetti C, et al. Herpes simplex virus-2 as a human papillomavirus cofactor in the etiology of invasive cervical cancer. *J Natl Cancer Inst* 2002; 94:1604.
- Society of Gynecologic Oncologists Education Resource Panel Writing group, Collins Y, Einstein MH, et al. Cervical cancer prevention in the era of prophylactic vaccines: a preview for gynecologic oncologists. *Gynecol Oncol* 2006; 102:552.
- Sutton GP, Bundy BN, Delgado G, et al. Ovarian metastases in stage IB carcinoma of the cervix: a Gynecologic Oncology Group study. *Am J Obstet Gynecol* 1992; 166:50.
- Torre LA, Bray F, Siegel RL, et al. Global cancer statistics, 2012. *CA Cancer J Clin* 2015; 65:87.
- Waggoner SE, Darcy KM, Tian C, Lanciano R. Smoking behavior in women with locally advanced cervical carcinoma: a Gynecologic Oncology Group study. *Am J Obstet Gynecol* 2010; 202:283.e1.
- Walboomers JM, Jacobs MV, Manos MM, et al. Human papillomavirus is a necessary cause of invasive cervical cancer worldwide. *J Pathol* 1999; 189:12.

- Wallin KL, Wiklund F, Luostarinen T, et al. A population-based prospective study of Chlamydia trachomatis infection and cervical carcinoma. *Int J Cancer* 2002; 101:371.
- Wang K, Zhou B, Zhang J, et al. Association of signal transducer and activator of transcription 3 gene polymorphisms with cervical cancer in Chinese women. *DNA Cell Biol* 2011; 30:931.
- Wang L, Gao R, Yu L. Combined analysis of the association between p73 G4C14-to-A4T14 polymorphisms and cancer risk. *Mol Biol Rep* 2012; 39:1731.
- Wang Q, Zhang C, Walayat S, et al. Association between cytokine gene polymorphisms and cervical cancer in a Chinese population. *Eur J Obstet Gynecol Reprod Biol* 2011; 158:330.
- Willoughby BJ, Faulkner K, Stamp EC, Whitaker CJ. A descriptive study of the decline in cervical screening coverage rates in the North East and Yorkshire and the Humber regions of the UK from 1995 to 2005. *J Public Health (Oxf)* 2006; 28:355.
- Workowski KA, Bolan GA, Centers for Disease Control and Prevention. Sexually transmitted diseases treatment guidelines, 2015. *MMWR Recomm Rep* 2015; 64:1.